REMARKS

I. Status of the Claims

Claims 1-10 are pending in the application, and claims 4-10 stand withdrawn. Thus, claims 1-3 are under consideration and stand rejected under 35 U.S.C. §112, first paragraph, and/or 35 U.S.C. §102, first paragraph. The specific grounds for rejection are set forth in detail below.

II. Objection

The disclosure is objected to for allegedly failing to provide a new CRF of the sequence listing including new SEQ ID NO: 64. A new sequence listing is being submitted herewith.

III. Rejection Under 35 U.S.C. §112, First Paragraph

Claim 3 remains rejected as lacking an enabling disclosure. Applicants in traverse, but in the interest of advancing the prosecution, the claim has been narrowed to remove certain disease states not indicated by the examiner to be enabled. In addition, applicants provide the declaration of Dr. Markus Hecker, one on the inventors, in support of the enablement for various other disease states for which the examiner has similarly not yet acknowledged enablement.

As discussed in the declaration, two related publications - Cattaruzza *et al.* (*Circ Res.* 95, 841-847, 2004) and Melchers *et al.* (Arthritis Rheum. 54, 3144–3151, 2006) indicate a higher risk for individuals homozygous for the T786C polymorphism of the human endothelial nitric oxide synthase (*nos-3*) gene for contracting coronary heart disease as well as rheumatoid arthritis are generally applicable to atherosclerosis. As explained, atherosclerosis is a systemic and chronic inflammatory disease of the vessel wall of large conductance as well as small resistance-

sized arteries (and arterioles) that may also present as transplant atherosclerosis, especially in solid organ transplants such as the heart, venous bypass graft vasculopathy and restenosis following angioplasty. The common denominator of both the classical type of atherosclerosis and its aforementioned variants is endothelial dysfunction, commonly referred to as a decreased bioavailability of endothelial cell-derived nitric oxide resulting in an exaggerated endothelial cell-leukocyte interaction and leading to chronic inflammation. Thus, depending on the location in the vasculature, atherosclerosis manifests itself as coronary artery or coronary heart disease which in the majority of cases leads to myocardial infarction and subsequently to heart failure. Atherosclerosis in the cerebral vasculature results in the majority of cases in stroke or multi-infarction dementia while in the periphery, especially in the arteries of the leg, it causes peripheral artery disease.

Therefore applicable diseases for which the decoy oligodeoxynucleotides disclosed in the above-captioned patent application may be used for as drugs encompass atherosclerosis in general together with its manifestations coronary heart (artery) disease, cerebrovascular disease and peripheral artery disease as well as the sequelae myocardial infarction and heart failure, stroke and multi-infarction dementia and gangrene, respectively. Indications for which the disclosed treatment modality is equally suited include transplant atherosclerosis or vasculopathy (chronic rejection), venous bypass graft atherosclerosis or vasculopathy and restenosis following angioplasty. In addition, rheumatoid arthritis and closely related chronic inflammatory diseases which like atherosclerosis can be traced back to endothelial dysfunction, are amenable to treatment with the disclosed decoy oligodeoxynucleotides.

In light of this evidentiary submission, reconsideration and withdrawal of the rejection is therefore respectfully requested.

IV. Rejection Under 35 U.S.C. §102(b)

Claims 1 and 2 are rejected as anticipated by Zhang *et al.* (1995). According to the examiner, the claims read on longer sequences including the eNOS promoter. Applicants have amended claim 1 to place an upper limit of about 30 bases on the size of the oligonucleotide, thereby further distinguishing the cited art. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

V. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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